REMARKS

Claims 1, 4, 7,13, 16, 20-21, and 24 have been withdrawn from consideration by the Examiner, who has alleged that the pending claims, as presently amended, are patentably distinct from the prior claims. In issuing this action, the Examiner claimed that the present claims are patentably distinct from the original invention, because they allegedly differ "with respect to one or more of ingredients and method steps from the method previously claimed" (see page 2-3 of Office Action dated February 7, 2005). In order to expedite prosecution, applicants are filing a divisional application of the instant application based on the "withdrawn" claims.

Claims 18, 29, 22, and 23 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Marasco et al. (WO 94/02610) in view of Marasco et al. (U.S. Patent No. 6,143,520).

Applicants respectfully submit that this rejection should be withdrawn for the following reasons.

The present invention provides a method of inhibiting a **specific undesired immune associated reaction** by using an intracellular antibody to bind to and inhibit a target molecule within the cell. More specifically, the invention as presently claimed takes advantage of the internal ribosome entry site (IRES) sequence to co-express both the heavy and light chains of the antibody.

The Examiner explicitly acknowledges that "WO 94/02610 **does not teach** the use of an internal ribosome entry site (IRES) for expression of the antibody, and **does not specifically exemplify** the use of lentivirus vectors" (Page 5, second paragraph; emphasis added). Another specific challenge presented by the use of intrabodies is the difficulty of achieving stoichiometric expression of the heavy and light chains of the intrabody. As specifically taught in the present invention, an IRES is also useful to obtain expression of the light and heavy chains in **equal** stoichiometric ratio, thereby permitting more effective assembly.

WO 94/02610 broadly teaches a generic method of using intrabodies. As acknowledged by the Examiner, nothing in the WO teaches or suggests the use of an IRES sequence. U.S. Patent No. 6,143,520 (hereinafter the '520) is directed to lentiviral vectors in which an IRES sequence is linked to a generic gene of interest, and is concerned with challenges presented by expressing high levels of genes. However, the '520 does not teach the specific advantages that can be obtained by

using an IRES sequence in expressing intrabodies in this specific area. Thus, the combination does not provide any motivation for using an IRES sequence in the claimed method.

In contrast, the present invention recognizes that specific intrabody targets pose specific challenges, and teaches specific solutions which are tailored to meet those challenges. The specification teaches the advantages of using an IRES sequence to solve the specific problem of a setting in which forced expression is desirable:

> Preferably the vectors of the present invention use internal ribosome entry site (IRES) sequences to force expression. As disclosed in Application No. 60/005,359, filed October 16, 1995, the use of IRES allows the "forced-expression" of the desired gene, for example, an sFv. In another embodiment, one can use an IRES to force a stoichiometric expression of light chain and heavy chain, e.g., in a Fab. This forced expression avoids the problem of "silencing" where cells expressing the desired protein are phenotypically not seen, which may occur with a wide range of gene products. (Page 34, lines 23-30 of the specification; emphasis added)

Another specific challenge presented by the use of intrabodies is the difficulty of achieving stoichiometric expression of the heavy and light chains of the intrabody. As specifically taught in the present invention, an IRES is also useful to obtain expression of the light and heavy chains in **equal** stoichiometric ratio, thereby permitting more effective assembly.

Accordingly, the specific embodiments of the present invention are in no way obvious from the combination of WO 94/02610 and the '520, both of which are directed to a different set of challenges than the present invention. Accordingly, applicants respectfully submit that this rejection should be withdrawn.

Accordingly, in view of the foregoing, applicants respectfully submit that all claims comply with 35 U.S.C. § 103.

In view of the foregoing, applicant respectfully submits that all claims are in condition for allowance. Early and favorable action is requested.

In the event that any additional fees are required, the PTO is authorized to charge our deposit account No. 50-0850.

Respectfully submitted,

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